

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>PC25529A</b>	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. <b>PCT/IB2004/003671</b>	International filing date (day/month/year) <b>08/11/2004</b>	(Earliest) Priority Date (day/month/year) <b>13/11/2003</b>
Applicant <b>PFIZER PRODUCTS INC.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amine acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

**4. With regard to the title,**

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**OCTAHYDROPHENANTHRENE HYDRAZINDE DERIVATIVES USEFUL AS GLUCOCORTICOID RECEPTOR MODULATORS**

**5. With regard to the abstract,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

**6. With regard to the drawings,**

- a. the figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D213/77 C07D417/12 A61K31/4402 A61P3/04 A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data, BEILSTEIN Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 380 223 B1 (DOW ROBERT L ET AL) 30 April 2002 (2002-04-30) the whole document -----	1-18

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&amp;\* document member of the same patent family

Date of the actual completion of the international search

25 January 2005

Date of mailing of the international search report

01/02/2005

Name and mailing address of the ISA

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Authorized officer

Johnson, C

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB2004/003671

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  

Although claims 14,15 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6380223	B1	30-04-2002	
		US 2002147336 A1	10-10-2002
		US 2004176595 A1	09-09-2004
		AU 776608 B2	16-09-2004
		AU 3316500 A	17-11-2000
		BG 106142 A	31-05-2002
		BR 0010138 A	22-01-2002
		CA 2372173 A1	09-11-2000
		CN 1349485 T	15-05-2002
		EA 4886 B1	26-08-2004
		EE 200100567 A	17-02-2003
		EP 1175383 A1	30-01-2002
		HR 20010804 A1	31-12-2002
		HU 0201243 A2	28-08-2002
		WO 0066522 A1	09-11-2000
		JP 2002543169 T	17-12-2002
		NO 20015272 A	28-12-2001
		NZ 514465 A	28-11-2003
		PL 353438 A1	17-11-2003
		SK 15442001 A3	04-03-2003
		TR 200103104 T2	21-05-2002
		ZA 200108846 A	28-10-2002

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

# PCT

To:

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/IB2004/003671

International filing date (day/month/year)  
08.11.2004

Priority date (day/month/year)  
13.11.2003

International Patent Classification (IPC) or both national classification and IPC  
C07D213/77, C07D417/12, A61K31/4402, A61P3/04, A61P3/10

Applicant  
PFIZER PRODUCTS INC.

### 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

### 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

10/209554  
International application No.  
PCT/IB2004/003671

2004 JAN 2006

**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-18 (part)

because:

☒ the said international application, or the said claims Nos. 14,15 relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-18 (part) are so unclear that no meaningful opinion could be formed (*specify*):

**see separate sheet**

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 14,15

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See separate sheet for further details

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-18
	No: Claims	
Inventive step (IS)	Yes: Claims	1-18
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-13, 16-18
	No: Claims	

**2. Citations and explanations**

**see separate sheet**



**III. Non-establishment of opinion**

Claims 14 and 15 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

The claims refer to isomers of the compounds of formula I. The word "isomer" includes positional isomers. It appears, however, from p. 5-6 of the description that only geometric and stereoisomers are intended to be covered by the claims. The claims have therefore only been searched and examined insofar as isomer means geometric and stereoisomers.

The term prodrug is not considered to define the matter for which protection is sought in a clear manner as required by Article 6 PCT. There are many possible functional groups present in the compound of formula I. The only information in the application as to which functional groups in which positions may be derivatised to give compounds having the attributes of prodrugs (i.e. compounds which are inactive per se, and which are broken down in the body to give active compounds) is given on p. 9, l. 10-20. In order to ascertain whether compounds outside this definition are within the scope of claim 1, the skilled man must perform in vivo tests, which is considered to go beyond the routine experimentation to be reasonably expected of him. The claims have only been searched and examined insofar as prodrug is as defined on p. 9, l. 10-20.

**V. Reasoned statement**

Reference is made to the following document:  
D1: US-B1-6 380 223

**Novelty**

The 2-substituent of the octahydrophenanthrene ring cannot be CONHNHheterocycle in D1 (see definition of R<sup>10</sup> in col. 6-7)..  
Claims 1-18 fulfil the requirements of Article 33(2) PCT.

**Inventive step**

The compounds of D1 are glucocorticoid receptor modulators useful in the treatment of obesity, diabetes and inflammation. The technical problem appears to be the provision of further compounds with this activity. In the absence of any documents showing the bioequivalence of the present -CONHNHheterocyclic

group with the R<sup>10</sup> group of D1 (e.g. the -NHNHCOheterocyclic group of ex. 406 or the -CONHalkyleneheterocyclic group of claim 1) in structurally similar compounds, it would not be obvious to make this modification to the compounds of D1 in the expectation that the activity would be maintained. Therefore those of the claimed compounds which have the desired activity are inventive. Claims 1-18 fulfil the requirements of Article 33(3) PCT.

**Industrial applicability**

Claims 1-13, 16-18 fulfil the requirements of Article 33(4) PCT.

No unified criteria exist in the PCT Contracting States for assessing whether present claims 14 and 15 are industrially applicable. The patentability can be dependent upon the formulation of the claims. For example, the EPO does not consider claims to the use of a compound in medical treatment to be industrially applicable, but allows claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

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